REMARKS

Applicants respectfully request entry of the amendment and reconsideration of the claims. Claim 20 has been amended to further clarify the invention. Claims 39-44 are newly presented. After entry of the amendment, claims 20 and 39-44 are pending.

Applicants submit the amended claim and newly presented claims are supported throughout the specification and do not raise any issues of new matter. See, for example, figure 6 and the specification at: page 10, lines 7-8; page 12, lines 24-27;page 13, lines 1-4; page 13, lines 30-32; and page 31, lines 8-10.

Sequence Rules

The Examiner objected to the specification because several portions of the text of the description were lacking reference to the SEQ ID NO of the amino acid sequence or nucleic acid sequence being described. Applicants have amended the specification to comply with the requirements of the sequence rules. Withdrawal of the objection is respectfully requested.

Double Patenting

The Examiner rejected claim 20 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-11 and 15-25 of U.S. Patent No. 5,859,206. Applicants acknowledge the rejection of the claims under the judicially created doctrine of obviousness-type double patenting. Applicants request that the Examiner hold this rejection in abeyance until indication of allowable subject matter.

Written Description

The Examiner rejected claim 20 under 35 U.S.C. § 112, first paragraph, as lacking written description. Applicants respectfully traverse this rejection.

The Examiner asserts one skilled in the art cannot reasonably visualize or predict what critical amino acid residues would structurally characterize the genus of polypeptides that would generate the claimed antibodies. Applicants disagree.

Applicants claims recite antibodies that bind a polypeptide that has at least 80% sequence identity to heregulin 2α having an amino acid sequence of SEQ ID NO: 11.

The written description requirement requires that Applicants' specification must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991). A written description of an invention involving a chemical genus requires a precise definition, such as by structure, formula ... of the claimed subject matter sufficient to distinguish it from other materials. Univ. of California v. Eli Lilly and Co., 43 USPQ2d 1398. 1405 (Fed. Cir. 1997) (emphasis added). Since one skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass, such a formula is normally an adequate description of the claimed invention. Id. at 1406 (emphasis added). Moreover, as noted in the Guidelines for Examination of Patent Applications Under 35 U.S.C. § 112, ¶1, "Written Description" Requirement ("the guidelines"), there is a "strong presumption" that an adequate written description of the claimed invention is present when the application is filed, 66(4) Fed Reg. 1099, 1105 (2001); see also, In re Wertheim, 191 USPQ 90,97 (CCPA 1976). The guidelines further state that "[(The examiner has the initial burden of presenting by a preponderance of evidence why a person skilled in the art would not recognize in an applicant's disclosure a description of the invention defined by the claims." 66(4) Fed. Reg. at 1107; 191 USPQ at 97, (emphasis added).

Compliance with the written description requirement does not require an applicant to describe exactly the subject matter claimed; rather, the description must clearly allow a person of ordinary skill in the art to recognize that he or she invented what is claimed. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991). The test is whether the originally filed specification reasonably conveys to a person having ordinary skill in the art that applicant had possession of the subject matter later claimed. In re Kaslow, 217 USPQ 1089 (Fed. Cir. 1991). Moreover, in order to have possession of members of a claimed genus, the specification need not describe all of the species that the genus encompasses. Amgen Inc. v. Chugai Pharmaceutical Co., 18 USPQ2d 1016, 1027 (Fed. Cir. 1991).

In contrast to the Examiner's contention, Applicants have described a heregulin 2α polypeptide both structurally and functionally. Applicants have described a polypeptide having a sequence of SEQ ID NO: 11. Applicants have also described variants of this polypeptide having at least 80% sequence identity to a polypeptide having sequence of SEQ ID NO: 11. Applicants

have further characterized these polypeptides as stimulating the tyrosine phosphorylation of $p185^{HER2}$. Applicants have shown that purified HRG2-α stimulate growth of $p185^{HER2}$ bearing cells and not EGF receptor bearing cells. See Figure 7 and page 86 in the specification.

Moreover, Applicants have further characterized this molecule by identifying the structural and functional domains such as the transmembrane domain and the EGF motif as described in Figure 6 and at pages 82 to 84 in the specification. This EGF motif of heregulin 2α is aligned with other human EGF related proteins in Figure 6. This alignment shows that the 6 cysteine residues in heregulin 2α EGF domain as well as the number of amino acids between the cysteines are conserved. This domain is similar to other EGF growth factor domains.

Applicants submit that one of skill in the art reading the specification would be able to viusalize the members of the genus of polypeptides that generate the antibodies as claimed based on both the structural and functional characterization of the polypeptides.

In view of the foregoing, Applicants assert the specification adequately describes the common structural and functional attributes of the genus of polypeptides that generate the claimed antibodies. Moreover, Applicants claims couple the common structural attributes to a functional attribute of the polypeptide (stimulating tyrosine phosphorylation of $p185^{HER2}$ receptors) such that one skilled in the art to would be able visualize or predict the genus of polypeptides that generate the claimed antibodies. Accordingly, Applicants submit the claims fully comply with the requirements of written description. Withdrawal of the written description rejection is respectfully requested.

Enablement

The Examiner rejected claim 20 under 35 U.S.C. § 112, first paragraph, as lacking an enabling disclosure. Applicants respectfully traverse this rejection.

The Examiner asserted the specification lacked guidance as to what minimal structural requirements are necessary to successfully generate antibodies that bind HRG2-α polypeptide. Applicants respectfully disagree.

Applicants have directed the claims to antibodies that specifically bind a polypeptide having at least 80% sequence identity to a polypeptide having the sequence of SEQ ID NO: 11, wherein the polypeptide stimulates tyrosine phosphorylation of $p185^{HER2}$ receptors. Applicants

submit that the specification provides sufficient disclosure to enable the production of specific antibodies raised against specific antigens. Applicants disclose common structural attributes coupled to a functional attribute that allows one skilled in the art to visualize or predict the genus of polypeptides that generate the claimed antibodies. For example, Applicants disclose that SEQ ID NO:11 comprises 6 cysteine residues characteristically positioned over a span of approximately 40 amino acids (the EGF motif). Processing of the proform of the polypeptide encoded by SEQ ID NO:11 yields a mature form of the protein comprising the EGF motif. See specification at page 31, lines 8-10. The EGF motif has homology to EGF domains that form a three loop, 3 disulfide bonded signature structure. Polypeptide isolated from the clone stimulate tyrosine phosphorylation of $p185^{HER2}$ receptors but not of EGF receptors. See Example 7 and Figure 7.

Based on this disclosure and the fact that the production of antibodies against a characterized antigen is a mature technology where the level of skill is high and advanced, Applicants assert one of skill in the art is enabled to make antibodies as claimed. Withdrawal of the enablement rejection is respectfully requested.

Conclusion

In view of the above amendments and remarks, Applicants respectfully request a Notice of Allowance. If the Examiner believes a telephone conference would advance the prosecution of this application, the Examiner is invited to telephone the undersigned at the telephone number listed below.

Respectfully submitted,

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